REMARKS

In the instant Action, claims 17-19, 26 and 31-32 are listed as pending and all claims are finally rejected. Applicants respectfully point out however, that claim 22 is also still pending in the application. Claims 17, 22 and 26 are amended and claims 18 and 19 are canceled in this reply. Claims 1-16, 20-21, 23-25, 27-30 and 33-40 were previously canceled and amendments to claims 31 and 32 were previously presented. Applicant expressly reserves the right to reclaim the canceled subject matter in a subsequent application.

Claim 17 is currently amended to incorporate the limitations of claim 19; claim 1 now recites the combination of Compound A and doxorubicin. Support for this amendment may be found in the claims as originally filed, in the Examples and in the Figures. Claims 22 and 26 are amended to correct claim dependencies due to cancellation of claims. Applicants submit that the amendments do not introduce new matter.

CLAIM REJECTIONS

1. Claim Rejections – 35 U.S.C. § 103(a)

1A. Rejection of claims 17-19 under 35 U.S.C. 103(a)

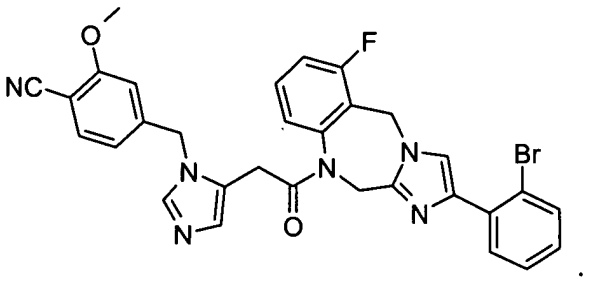
On pages 2-6 of the instant Action, the Examiner has maintained the rejection of claims 17-19 under 35 U.S.C. § 103(a) as being unpatentable over Gordon *et al.* (PCT International Publication WO 00/39130, referred to hereinafter as "Gordon") in light of Rybak (PCT International Publication WO 01/64197, referred to hereinafter as "Rybak"). In brief, the Examiner alleges that as Gordon discloses the farnesyl transferase inhibitor (FTI) of instant claims 17-19, and as Rybak discloses therapeutic combinations of anthracyclines and FTIs, it would have been obvious to the skilled artisan to provide a pharmaceutical composition comprising an FTI according to Gordon and an anthracycline such as doxorubicin to treat NPC.

The complete details of the Examiner's comments are found on pages on pages 2-6 of the instant Action; these comments are not reiterated in full in this reply.

1B. Claim 17 is not obvious over Gordon in light of Rybak

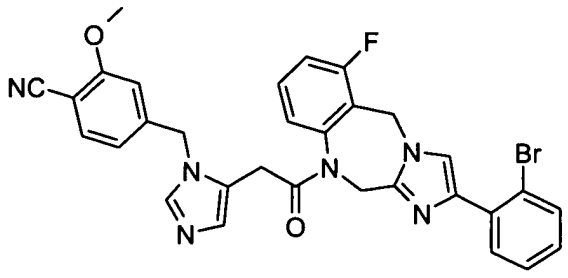
Applicants again respectfully submit that the invention of instant claim 17 is not obvious over Gordon in light of Rybak. Applicants incorporate all arguments presented in reply to this rejection from the previous replies (mailed September 26, 2007) and offer the following additional comments.

Firstly, Applicants note that claim 17 is now directed to a composition comprising one particular anthracycline and one particular farnesyl transferase inhibitor: doxorubicin and



;

Applicants again note that neither Gordon nor Rybak teach or suggest the **particular** FTI/doxorubicin combination recited in instant claim 17. Gordon teaches thousands of FTI compounds; Applicants submit that the Examiner has again failed to point out the teachings of Gordon that would guide the skilled artisan to select ***the*** single FTI compound from among the multitude of compounds presented. This defect is not cured by Rybak as Rybak discloses even more FTI compounds and fails to provide any data or teachings to direct the skilled artisan to select particular compounds. There is simply no teaching or suggestion in Gordon and/or Rybak that would lead the skilled artisan to select any one compound over any other compound presented, let alone the **particular** FTI/doxorubicin combination of instant claim 17. It is Applicants' teaching

that identifies  and doxorubicin as a desired combination, a selection that was unknown and unappreciated by Gordon and/or Rybak. As recently decided in Boston Scientific v Johnson & Johnson (No. C 02-00790, 2007 WL 2408870 at *13-14 (N.D. Cal. Aug. 21, 2007)), a passing reference to a possible solution does not necessarily imply that it is a viable solution.

Applicants again submit that a reasonable expectation for success must lead to a predictable result and must be more than the presentation of a laundry list of options with no guidance provided as to which option to choose. Applicants submit that a reasonable expectation of success is not automatically established where the prior art discloses many alternative routes. Art that provides many opportunities for erroneous or unsupported combinations and fails to teach success cannot make obvious the clear choice to make. See Takeda Chemical v Alphapharm (492 F.3d 1350, 1356 (Fed. Cir. 2007)):

"Rather than identify predictable solutions [for antidiabetic treatment], the prior art disclosed a broad selection of compounds ***any one of which*** could have been selected as a lead compound for further investigation." (emphasis added)

In a similar vein, neither Gordon nor Rybak, nor the combination of the two, which provide thousands of possible FTI compounds and anthracycline compounds, provide any direction to select the ***particular*** FTI/doxorubicin combination as described in instant claim 17. Absent the teaching of the instant invention, the skilled artisan could only guess at which FTI compound to combine with which anthracycline compound. With so many options presented in Gordon and/or Rybak, the options to choose a FTI/anthracycline combination *other* than that of instant claim 17 far outweigh the teaching to choose the combination of instant claim 17. Applicants submit that the

Examiner has again failed to establish a prima facie case for obviousness as required under 103(a).

Applicants submit that because neither Gordon nor Rybak nor the combination of the two, actually provide any data demonstrating the advantage of the combination of an FTI and doxorubicin, Gordon and Rybak cannot support the Examiner's argument that the combination of claim 17 "is likely to be obvious". It is Applicants' data that provides the missing link, demonstrating that the hoped for synergy in fact can occur and it is Applicants' data that shows that the particular combination of claim 17 is advantageous.

1C. Request for withdrawal of rejection of claim 17 under 35 U.S.C. § 103(a)

Applicants submit that, for reasons cited above, claim 17 is in no way made obvious by Gordon in light of Rybak. Applicants request the reconsideration and withdrawal the rejection of claim 17 under 35 U.S.C. § 103(a).

2. Claim Rejections – 35 U.S.C. § 103(a)

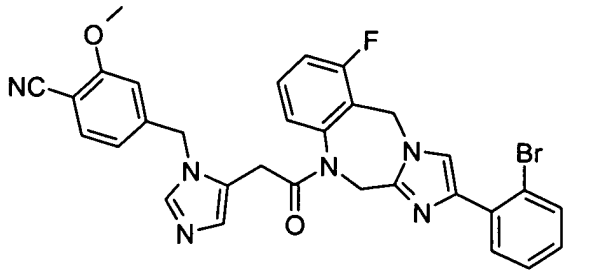
2A. Rejection of claims 22, 26, 31 and 32 under 35 U.S.C. 103(a)

On pages 6-8 of the instant Action, the Examiner maintains the rejection of claims 22, 26, 31 and 32 under 35 U.S.C. § 103(a) as being unpatentable over Gordon in light of Rybak in further view of Porter *et al.* (Acta Otolaryngol, 1994, 114:105; referred to hereinafter as "Porter"). In brief, the Examiner alleges that as Gordon and Rybak disclose the FTI/anthracycline combination of the instant invention and Porter discloses a study in which 73% of NPC investigated exhibited increased expression of *ras*, it would have been obvious to the skilled artisan to use a combination of an FTI and an anthracycline to treat NPC. The complete details of the Examiner's comments are found on pages on pages 6-8 of the instant Action and are not reiterated in full in this reply.

2B. Claims 22, 26, 31 and 32 are not obvious over Gordon in light of Rybak and Porter

Applicants respectfully submit that the invention of claims 22, 26, 31 and 32 is not obvious over Gordon in light of Rybak and Porter.

Applicants respectfully submit that for the reasons cited above, the Examiner has failed to present a *prima facie* case for obviousness against instant claim 17, *i.e.*, the **particular** FTI/doxorubicin combination where the FTI is



This failure to identify the particular FTI/doxorubicin combination of claim 17 is not cured by Porter as Porter simply demonstrates that some NPC carcinomas exhibit high levels of *cmyc* or *ras*. Because the method of use of claims 22, 26, 31 and 32 utilizes the particular FTI/doxorubicin combination of claim 17, Gordon, Rybak and Porter fail to teach all aspects of the claims. As recited in the MPEP at 2143.03, "to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F2.d 981, 180 USPQ 580 (CCPA 1974)".

Applicants further submit that this combination of references fails to support a *prima facie* case of obviousness because the references do not teach or suggest to the skilled artisan that the presence of *ras* protein is the key teaching to *knowing* that FTIs and anthracyclines will obviously work in an additive fashion as anticancer agents against NPC. Gordon discusses that intervention of the function of *ras* mediated signal transduction by prenyl transferase inhibitors may be useful in the treatment of cancer. Rybak also postulates that farnesyl transferase inhibitors may be useful as anticancer agents to treat tumors in which *ras* contributes to transformation.

However, Gordon is silent as to the use of anthracyclines as anti-tumor agents at all and Rybak fails to teach or suggest that anthracyclines effect anti-tumor activity via a *ras* mediated pathway. Porter does not cure this defect of Gordon and Rybak as Porter fails to teach or suggest that anthracyclines or FTIs exert a cellular effect upon *ras* mediated pathways or that such an effect is key to the anti-tumor activity attributed to

these compounds. Thus the combination of Gordon, Rybak and Porter do not and cannot teach or suggest to the skilled artisan that the doxorubicin/FTI combination of claim 17 will necessarily result in an increased anti-tumor effect via a *ras* mediated pathway.

2C. Request for withdrawal of rejection of claims 22, 26, 31 and 32 under 35 U.S.C. § 103(a)

Applicants submit that, for reasons cited above, claims 22, 26, 31 and 32 are in no way made obvious by Gordon in light of Rybak and Porter. Applicants request the reconsideration and withdrawal the rejection of claims 22, 26, 31 and 32 under 35 U.S.C. § 103(a).

Reconsideration of the instant Office Action, entry of the amendments submitted herewith, and allowance of all pending claims are respectfully requested. Prompt and favorable action is solicited.

Respectfully submitted,

Date: 9/23/09

Pamela C. Ball

Pamela C. Ball
Agent for Applicant(s)
Reg. No. 53,963

Biomeasure, Incorporated
27 Maple Street
Milford, MA 01757-3650
(508) 478-0144 Telephone
(508) 473-3531 Facsimile